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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,254	06/25/2003	Chih-Ming Chen	300.1003CON	3690

23280 7590 06/06/2006

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 06/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,254	CHEN ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *76-84,88 and 89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *76-84 and 88-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Remarks filed 3/31/06 is acknowledged. Claims **76-84 and 88-89** are pending in this application. Claims 1-75 and 85-87 stand cancelled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 76-84 and 88-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 5, 837,379 to Chen et al by itself or in view of Cheng et al (Evaluation of Sustained/Controlled Release dosage forms of 3-Hydroxy-3-Methylglutaryl-Coenzyme A(HMG-CoA) Reductase Inhibitors in Dogs and Humans, Pharmaceutical Research (1993), 10:1683-1687).

Chen et al disclose a once a day controlled release pharmaceutical tablet comprising (a) a homogeneous compressed core of granules produced in a fluidized bed, said core said core comprising: (i) a medicament; (ii) a water soluble osmotic compound; (iii) one or more osmotic

polymers wherein one of the osmotic polymers is a water swellable osmotic polymer; and (b) a membrane coating which completely covers said core tablet which comprises a mixture of: (i) a water insoluble pharmaceutically acceptable polymer; and (ii) an enteric polymer. See abstract, examples, and claim 1. The tablet provides a controlled and extended-release pharmaceutical dosage form in order to maintain therapeutic serum levels of medicaments and to minimize the effects of missed doses of drugs caused by a lack of patient compliance.

Chen teaches medicaments, which are suitable for use in the dosage form, are water soluble to practically insoluble in water. Chen teaches various water-insoluble medicaments that may be utilized for therapeutic dose levels including instant lovastatin. See column 2, line 64. The core composition will contain one or more osmotic polymers including water-soluble polyvinyl pyrrolidone having a weight average molecular weight of 25,000 to 200,000, hydroxy propyl cellulose, and hydroxyethylcellulose, etc. Note this reads on claim 88. The membrane coating completely covers said core comprises a water insoluble pharmaceutically acceptable polymer in combination with an enteric polymer. Note this reads on claim 89. The composition may additionally have dispersants, lubricants, dyes, and other additives that are conventionally utilized in the art. See column 5, lines 63-65. More specifically, Chen et al teach that the medicament granules contain povidone (osmotic polymer), lactose (osmotic agent), and sodium lauryl sulfate (surfactant). The granules are compressed with lactose, Polyox WSR, and Myvaplex and coated with a color coating contains dye, sodium chloride, and water. The color coating is coated with a sustained release coating; followed by an enteric coating containing HPMC phthalate, pore forming agent, talc, and plasticizer. See examples. Lastly it should be noted that lovastatin hydrolyzes in vivo to form its acid form, lovastatin acid.

Chen does not exemplify lovastatin in the controlled release device nor explicitly teach the instant functional limitations.

Cheng et al teach controlled release device containing lovastatin and a sustained release matrix for the treatment of hypercholesterolemia. Cheng discloses that lovastatin hydrolyzes in vivo to form its corresponding beta-hydroxyacid, which are potent inhibitors of HMG-CoA reductase. See page 1683. Further, Cheng discloses that the liver, the target organ, more efficiently extracts lovastatin and simvastatin than their corresponding beta-hydroxyacid. Thus, the use of controlled release device allows for an equal or better therapeutic value. Table II teaches the total HMG-CoA reductase inhibitors (lovastatin and its acid form) pharmacokinetic parameters (AUC, the Cmax, Tmax, AUC ratio of 0.94, 1.03, 0.43, and 0.52, and Cmax ratio of 0.66, 0.64, 0.16, and 0.13) in dogs receiving various lovastatin dosage forms. See page 1685. Table V teaches the pharmacokinetics of simvastatin administered to humans. See page 1687.

Firstly, it is deemed obvious to one of ordinary skill in the art at the time the invention was made to look to the guidance provided by Chen et al and include the instant lovastatin in the controlled release dosage form. One would have been motivated to do so since Chen teaches a variety of medicaments that would benefit from the use of controlled release formulation in order to maintain a therapeutic level of the drug and teaches the instant lovastatin as one of the suitable medicaments. Therefore, a skilled artisan could reasonably expect similar results by including lovastatin in Chen's controlled release device.

With regard to the instantly claimed Tmax and functional limitations, it is the examiner's position that Chen's controlled release device would meet the instant functional limitations since Chen's controlled release device is substantially similar in structure and formulation to

applicant's dosage form described in the specification; in particular note Table I of instant specification wherein applicant's teaches the general formula of Table I provides the functional limitation. It is noted that the applicant does not claim the controlled release structure in the claims and thus the examiner is permitted to look to the instant specification to define the controlled release device in terms of structure that provides the instantly claimed functional limitations. Therefore, it is the examiner's position that both would function similarly if not the same since the structures of the instant invention and that of the prior art are the same.

Secondly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further look at Cheng et al and specifically utilize lovastatin in Chen's controlled release device. One would have been motivated to do so since Cheng teaches lovastatin is an effective drug in reducing cholesterol serum levels in humans and it is beneficial to utilize a controlled or sustained release device. Therefore, Cheng provide a further motivation to specifically utilize lovastatin as the drug of choice if one desired to treat cholesterol serum levels. Further, although Cheng utilizes an animal model for drawing the conclusions that controlled release devices provide a better efficacy of lovastatin, it is conventional in the pharmaceutical research to draw conclusions from animal models and apply them to humans.

Response to Arguments

Applicant argues that Chen teaches an exhaustive list of possible agents and thus one would not have been motivated to particularly select a single species such as lovastatin. Applicant argues that the size of the genus is not sufficiently small as to render the each member inherently disclosed. Applicant argues that Chen does not provide any motivation to select lovastatin or that species disclosed are structurally similar. Applicant argues that nifedipine is not

structurally similar to lovastatin and thus one would not expect that they would provide similar pharmacological activities.

Applicant argues that Table 1 of the instant specification is not similar to Chen's controlled release device. Applicant argues that Chen fails to disclose, teach, or even hint of the Tmax range. It is argued that Chen does not teach a desirability of releasing lovastatin in a controlled rate. Applicant argues that Chen does not teach increasing the bioavailability of lovastatin.

Applicant's arguments filed 3/31/06 have been fully considered but they are not persuasive. Firstly, the examiner points out that applicant's arguments with regard to genus-species is not relevant to the instant rejection since the rejection has not made an anticipation rejection and rather made under obviousness. Thus a skilled artisan need not "immediately envisage" the use of lovastatin in the dosage form since this is a requisite for anticipation and not obviousness. The examiner has not purported that a skilled artisan would immediately envisage the use of lovastatin, rather the examiner's position is that it is obvious to use lovastatin since Chen teaches lovastatin as a suitable drug to use in the controlled release dosage form. Therefore, the motivation of utilizing lovastatin is within the disclosure of Chen itself. Moreover, a skilled artisan would expect that the Chen's controlled release dosage form would function the same irrespective of the drug utilized since Chen's general discloses is to a controlled release device that provides controlled release of a medicament in order to maintain therapeutic serum levels of the medicament.

Secondly, the examiner has not purported there is a structural similarity with nifedipine and lovastatin. The examiner notes the difference in pharmacological effects and the structure of

the compounds. The examiner's position is that Chen's controlled release device is similar, if not same, to the instantly claimed controlled device and thus the prior art's controlled release device will meet the instantly claimed functional limitations including the instant Tmax. The examiner points out that United States Patent Office does not have the facilities to test products for the properties they may or may not impart, i.e. the pharmacological properties provided by Chen's controlled release dosage form. Thus, the examiner must make a sound rationale as to why the prior art's dosage form is capable of meeting the instantly claimed functional limitations including the instantly claimed Tmax.

In instant case, the claims broadly recite a "controlled release oral dosage form" without any structurally distinguishing features. Therefore the examiner refers to the specification to provide for a general formula, i.e. Table I and examples, wherein the applicant states that the general controlled release dosage form described in Table I provide a Tmax of 10-32 hours. The examiner points out that Chen teaches a core containing the drug, povidone (a water-swellable polymer), an osmotic agent (lactose), and sodium lauryl sulfate (surfactant) in applicant's amount disclosed in Table I. The core is coated with a color coating containing a dye and sodium chloride (osmotic agent). The prior art's color coat is comparable to applicant's seal coat. Then a sustained release coating containing Eudragit S (enteric polymer), and a plasticizer in applicant amount disclosed in Table I. The prior art's sustained release coat is comparable to applicant's inner coat. Lastly, the tablet is again coated with an enteric coating polymer containing an enteric polymer, a pore-forming agent (channeling agent), acetyltributyl citrate (plasticizer). The prior art's enteric coat is comparable to applicant's overcoat. Therefore, it can be seen that this device

is the same as the described in instant specification of the preferred controlled release device that provides functional limitations of the instant application.

Again, the examiner has provided a rationale that the prior art would function in the same or similar manner as claimed; thus the burden has shifted to applicant to prove otherwise. As noted in *In re Best*, the Patent Office can require the applicant to prove that a subject matter shown in the prior art does not possess a characteristic when there is reason to believe that the functional limitation asserted to be critical in establishing novelty in the claimed subject matter, is possessed by the prior art. The examiner suggests the applicant compare Chen's device with the instant invention to substantiate applicant's arguments. The applicant has not provided any evidence that Chen would not be capable of providing the instantly claimed functional limitations.

With regard to applicant's argument that the examiner has relied in hindsight reasoning, the examiner believes that hindsight motivation has not been applied since Chen's disclosure, itself, provide the motivation to utilize lovastatin. The examiner points out that Chen need not exemplify every single drug taught to be suitable in order to render the instant invention obvious. Disclosed examples and preferred embodiments do not constitute a teaching away form the broader disclosure or nonpreferred embodiment". In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

Applicant argues that the instant invention is directed to increasing bioavailability of lovastatin and Cheng et al teach the controlled release device decreases bioavailability. Applicant further argues that SRT8 and SRT14 are irrelevant since Cheng states that SRT8 and SRT14

dosage forms showed little evidence in vivo. Applicant argues that Cheng does not teach the instantly claimed Tmax.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Instant case, although Chen et al suggests the use of lovastatin, the examiner relies on Cheng to provide further motivation to specifically select lovastatin and utilize in the controlled release device. As set forth in the rejection, Cheng teaches lovastatin is an effective drug in reducing cholesterol serum levels in humans and it is beneficial to utilize a controlled or sustained release device. Therefore, a skilled artisan would have been motivated to utilize lovastatin, if one wanted to treat high cholesterol serum levels. Therefore, the selection of a particular drug for use in the composition is considered prima facie obvious since the selection depends on the symptoms and disease being treated.

With regard to the specific teaching of Cheng, it is acknowledged that the formulations of CRS8 and CRS14 taught by Cheng both decreased bioavailability of lovastatin compared to the immediate release (CT). However, it is the examiner's position that SRT8 and SRT14 are relevant. Although Cheng teaches that SRT8 and SRT14 were dropped from further testing, nonetheless SRT14 is disclosed as having a higher bioavailability of lovastatin compared to the immediate dosage form. A known composition does not become patentable simply because it has been described as inferior compared to another product for the same use. See in re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). In instant case, Cheng teaches a

sustained release device with lovastatin that has a higher bioavailability than the immediate release as seen in Table II.

Lastly with regard to applicant's argument that Cheng does not teach the instantly claimed Tmax, the examiner points out this is not the premise of the rejection. Cheng is not relied upon to teach the instantly claimed Tmax since it is the examiner's position that Chen's controlled device provides the same Tmax. The examiner relies on Cheng merely to further provide motivation to select lovastatin and reasonably expect success. A skilled artisan would have reasonably expected success since Chen suggests the use of lovastatin in the controlled release device and Cheng teaches it is beneficial to administer lovastatin using a controlled or sustained release device to reduce cholesterol serum levels in humans.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 76-84 and 88-89 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,916,595. Although the conflicting claims are not identical, they are not patentably distinct from each other because since they encompass similar subject matter.

US '595 is directed to a controlled release formulation containing alkyl ester of a hydroxy substituted naphthalene compound, said formulation comprising: (a) a compressed tablet core which contains an alkyl ester of a hydroxy substituted naphthalene compound, a pharmaceutically acceptable, water swellable polymer and an osmotic agent; and (b) an outer coating layer which completely covers the osmotic core and comprises a pH sensitive coating agent, a channeling agent and a water insoluble cellulosic polymer used at a weight ratio of 0.1:1 to 0.75:1 and at a combined coating weight of 0.5-5% by weight. Note the pH sensitive coating is a enteric polymer.

Instant application is directed to a controlled release oral solid dosage form for the reduction of serum cholesterol levels containing lovastatin and a controlled release carrier wherein the said dosage form has certain functional limitations upon consumption of said dosage form.

The difference between the instant claims and that of US patent is that '595 does not claim the functional limitation of the controlled release device as seen in instant application. The instant claims are directed to a broad recitation of "controlled release carrier" without a specific structure and US patent is directed to a specific carrier having a compressed core comprising the medicament and water-swellable polymer and outer coating layer comprising a water insoluble polymer and an enteric polymer. Furthermore, the dependent claims of US patent claim a seal coat and an overcoat. The instant specification provides a general formula that provides the instantly claimed functional limitations, which comprises a compressed core comprising the medicament, antioxidant, and water-swellable polymer and outer coating layer comprising a water insoluble polymer. Further, the device optionally can include a seal coat and overcoat.

Thus, it is the examiner's position that the controlled dosage form of US patent '595 would provide the instantly claimed functional limitation including the instant Tmax.

Response to Arguments

Applicant states that a Terminal Disclaimer over 5,916,595 has been filed. However, the examiner notes that applicant has not filed a Terminal Disclaimer and thus the rejection will be maintained.

Claims 76-84 and 88-89 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4-14 of US patent 6,485,748 in view of Cheng et al (Evaluation of Sustained/Controlled Release dosage forms of 3-Hydroxy-3-Methylglutaryl-Coenzyme A(HMG-CoA) Reductase Inhibitors in Dogs and Humans, Pharmaceutical Research (1993), 10:1683-1687). Although the conflicting claims are not identical, they are not patentably distinct from each other because since they encompass similar subject matter.

US '748 is directed to a controlled release tablet which comprises: (a) a homogeneous compressed core which comprises: (i) a medicament which is very slightly soluble to practically insoluble in water at 25.degree. C.; (ii) a water soluble osmotic compound (iii) one or more osmotic polymers which comprise poly (ethylene oxide); and (b) a membrane coating which completely covers said core tablet which comprises a mixture of a: (i) a water insoluble pharmaceutically acceptable polymer; and (ii) a pH dependent polymer such as an enteric coating polymer, the weight ratio of the pH dependent polymer to the water insoluble pharmaceutically acceptable polymer being 0.1:1 to 0.75:1.

Cheng et al teach controlled release device containing lovastatin and a sustained release matrix for the treatment of hypercholesterolemia. Cheng discloses that lovastatin hydrolyzes in vivo to form its corresponding beta-hydroxyacid, which are potent inhibitors of HMG-CoA reductase. See page 1683. Further, Cheng discloses that the liver, the target organ, more efficiently extracts lovastatin and simvastatin than their corresponding beta-hydroxyacid. Thus, the use of controlled release device allows for an equal or better therapeutic value. Table II teaches the total HMG-CoA reductase inhibitors (lovastatin and its acid form) pharmacokinetic parameters (AUC, the Cmax, Tmax, AUC ratio of 0.94, 1.03, 0.43, and 0.52, and Cmax ratio of 0.66, 0.64, 0.16, and 0.13) in dogs receiving various lovastatin dosage forms. See page 1685. Table V teaches the pharmacokinetics of simvastatin administered to humans. See page 1687.

Instant application is directed to a controlled release oral solid dosage form for the reduction of serum cholesterol levels containing lovastatin and a controlled release carrier wherein the said dosage form has certain functional limitations upon consumption of the said dosage form.

The difference between the instant claims and that of US patent is that '748 does not claim the functional limitation of the controlled release device as seen in instant application and is broadly directed to an insoluble medicament. The instant claims are directed to a broad recitation of "controlled release carrier" without a specific structure and US patent is directed to a specific carrier having a compressed core comprising the medicament and osmotic polymer and a membrane coating comprising a water insoluble polymer. The instant specification provides a general formula that provides the instantly claimed functional limitations, which comprises a compressed core comprising the medicament, antioxidant, and water-swellable

polymer and outer coating layer comprising an enteric polymer and water insoluble polymer. Thus, it is the examiner's position that the controlled dosage form of US patent '748 would provide the instantly claimed functional limitation including the instant Tmax.

With regard to specific selection of lovastatin, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further look at Cheng et al and specifically utilize lovastatin in the controlled release device. One would have been motivated to do so since Cheng teaches lovastatin is an effective drug in reducing cholesterol serum levels in humans and it is beneficial to utilize a controlled or sustained release device. Therefore, Cheng provide a further motivation to specifically utilize lovastatin as the drug of choice if one desired to treat cholesterol serum levels. Furthermore, one would have expected similar results since it lovastatin is a water-insoluble drug. US patent also defines lovastatin as a water insoluble drug.

Response to Arguments

Applicant argues that US '748 does not claim or teach a controlled dosage form that increases the bioavailability of lovastatin or instant Tmax. Applicant argues that the disclosure cannot be used as prior art in a double patenting rejection but can be used as a dictionary to learn the meaning of the term.

Applicant's arguments filed 3/31/06 have been fully considered but they are not persuasive. The examiner acknowledges the fact that in an obviousness double patenting rejection, the disclosure of the prior art cannot be used unless it is used to define a term. The examiner has not relied on the disclosure of US '748 and rather has relied on the instant application's disclosure, which is permitted. The examiner points out that the instant claims are broadly directed to lovastatin and a controlled release carrier, which provides a certain Tmax.

Thus, the examiner utilizes the *instant specification* to define the structure that provides the functional limitation. Table 1 of instant specification provides a general formula that provides the instantly claimed functional limitations, which comprises a compressed core comprising the medicament, antioxidant, and water-swellable polymer and outer coating layer comprising a water insoluble polymer. The controlled release dosage form of US 748 comprises medicament core with a polymer and a coating with an insoluble coating. Thus, it is the examiner's position that the controlled dosage form of US patent '748 would provide the instantly claimed functional limitation including the instant Tmax. Therefore, it is the examiner's position that the instant application and US patent are obvious variants of each other since the instant application claims a controlled release dosage form in terms of functional limitations and US '748 claims the controlled release dosage form in terms of a structure.

Claims 76-84 and 88-89 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-13, and 15 of U.S. Patent No. 5,837,379 in view of Cheng et al (Evaluation of Sustained/Controlled Release dosage forms of 3-Hydroxy-3-Methylglutaryl-Coenzyme A(HMG-CoA) Reductase Inhibitors in Dogs and Humans, Pharmaceutical Research (1993), 10:1683-1687). Although the conflicting claims are not identical, they are not patentably distinct from each other because since they encompass similar subject matter.

US '379 is directed to a once a day controlled release tablet which comprises: (a) homogeneous compressed core of granules produced in a fluidized bed, said core said core comprising: (i) a medicament; (ii) a water soluble osmotic compound; (iii) one or more osmotic polymers wherein one of the osmotic polymers is a water swellable osmotic polymer; and (b) a

membrane coating which completely covers said core tablet which comprises a mixture of: (i) a water insoluble pharmaceutically acceptable polymer; and (ii) an enteric polymer.

Cheng et al teach controlled release device containing lovastatin and a sustained release matrix for the treatment of hypercholesterolemia. Cheng discloses that lovastatin hydrolyzes in vivo to form its corresponding beta-hydroxyacid, which are potent inhibitors of HMG-CoA reductase. See page 1683. Further, Cheng discloses that the liver, the target organ, more efficiently extracts lovastatin and simvastatin than their corresponding beta-hydroxyacid. Thus, the use of controlled release device allows for an equal or better therapeutic value. Table II teaches the total HMG-CoA reductase inhibitors (lovastatin and its acid form) pharmacokinetic parameters (AUC, the Cmax, Tmax, AUC ratio of 0.94, 1.03, 0.43, and 0.52, and Cmax ratio of 0.66, 0.64, 0.16, and 0.13) in dogs receiving various lovastatin dosage forms. See page 1685. Table V teaches the pharmacokinetics of simvastatin administered to humans. See page 1687.

Instant application is directed to a controlled release oral solid dosage form for the reduction of serum cholesterol levels containing lovastatin and a controlled release carrier wherein the said dosage form has certain functional limitations upon consumption of the said dosage form.

The difference between the instant claims and that of US patent is that '379 does not claim the functional limitation of the controlled release device as seen in instant application and is broadly directed to a medicament. The instant claims are directed to a broad recitation of "controlled release carrier" without a specific structure and US patent is directed to a specific carrier having a compressed core comprising the medicament and osmotic polymer and a membrane coating comprising an enteric polymer and water insoluble polymer. The instant

specification provides a general formula that provides the instantly claimed functional limitations, which comprises a compressed core comprising the medicament, antioxidant, and water-swellable polymer and outer coating layer comprising a water insoluble polymer and an enteric coating. Thus, it is the examiner's position that the controlled dosage form of US patent '379 would provide the instantly claimed functional limitation including the instant Tmax.

With regard to specific selection of lovastatin, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further look at Cheng et al and specifically utilize lovastatin in the controlled release device. One would have been motivated to do so since Cheng teaches lovastatin is an effective drug in reducing cholesterol serum levels in humans and it is beneficial to utilize a controlled or sustained release device. Therefore, Cheng provide a further motivation to specifically utilize lovastatin as the drug of choice if one desired to treat cholesterol serum levels.

Response to Arguments

Applicant argues that US '379 does not claim or teach a controlled dosage form that increases the bioavailability of lovastatin or instant Tmax.

Applicant's arguments filed 3/31/06 have been fully considered but they are not persuasive. As discussed above, it is the examiner's position that the controlled release device of US '379 would provide the same functional limitation as claimed. It is the examiner's position that the applicant has not provided any persuasive evidence or arguments other than "the claims fail to teach or suggest the Tmax"; thus the rejection is maintained.

Conclusion

All the claims are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharmila S. Gollamudi
Examiner
Art Unit 1616

Johann Richter, Ph.D. Esq.
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